D2

--26. (New) A composition comprising the agent of claim 20 and a pharmaceutically acceptable carrier.--

REMARKS

Claims 1-25 were pending in the subject application. Applicants have hereinabove canceled claims 1-19 and 23-25 without prejudice or disclaimer to applicants right to pursue the subject matter of these claims in a later-filed application. In addition, applicants have amended claim 20 and added new claim 26. Support may be found inter alia in the specification as follows: Claim 20: page 21, lines 22-35; Claim 26: page 24, lines 28-31. Claims 20 and 26 do not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 20-21 and 26 will be pending.

Election/Restriction:

The Examiner stated that the applicant's election with traverse of Group V (claims 20-21) in Paper No. 10 is acknowledged. The Examiner alleged that applicants traversal is on the ground(s) that all groups are "related" and therefore should be rejoined. The Examiner stated that this is not found persuasive because each of the separate groups are allegedly distinct because they have acquired a separate status in the art as shown by their different classification, they are directed toward patentably distinct products, or are directed to methods with different goals, starting materials and /or method steps. The Examiner alleged that there is a proper distinction between these groups, since each product is not required in order for the other to exist. The Examiner stated that because these inventions are distinct for the reasons given above and in the previous Office action, and the non-

coextensiveness of the search and consider each of these separable groups, the requirement is still deemed proper. The Examiner stated that the requirement is still deemed proper and is therefore made FINAL. The Examiner stated that claims 1-19 & 22-25 are withdrawn from further consideration pursuant to 37 CFR 1.42 (b), as allegedly being drawn to a non-elected inventions, there being no allowable generic or linking claim. The Examiner stated that the applicant timely traversed the restriction (election) requirement in Paper No.10. The Examiner stated that this application contains claims 1-19 & 22-25 allegedly drawn to an invention non-elected with traverse in Paper No.10. The Examiner stated that a complete rely to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Rejection under 35 U.S.C. §112, first paragraph:

The Examiner rejected claims 20-21 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a binding assay using the specific purified ERAB polypeptide of SEQ ID NO 2 and the amyloid-beta polypeptide structurally described on pages 1-2 of the specification, allegedly does not reasonably provide enablement for any method in which the required components necessary to practice the method are structurally and functional uncharacterized (i.e., as it relates to generic uncharacterized ERAB polypeptides). The Examiner alleged that the specification does not enable any person skilled in the art to which it pertains, or with which it is mostly nearly connected, to make and use the invention commensurate in scope with these claims. The Examiner alleged that the name "ERAB polypeptide" (as it relates to how it is defined on pages 14-17 of the specification) does not

sufficiently characterize and enable the polypeptides that are required to practice the instant invention, because the inclusion of any "variant or portion thereof", or "insertions, deletions and substitutions therof", or any biologically functional equivalent protein, within the definition of a ERAB polypeptide sets forth little structural and functional characteristics. The Examiner alleged that the specification does not teach which particular amino acids are critical for any ERAB protein's function, nor how to distinguish such from any different polypeptide sequence that possesses none of the desired functions of the instant invention. The Examiner alleged that random modifications, mutations, substitutions, additions, deletions or truncations of different ERAB-related polypeptides would be expected by the skilled artisan to result in generation of inactive proteins, and therefore, a method that does not work. The Examiner citing Rudinger on page 3 recites that "it is impossible to attach a unique significance in different peptide sequences, or even in different positions of the same sequence". The Examiner alleged that Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted a priori but must be determined from case to case by painstaking experimental study". The Examiner alleged that therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any ERAB protein's function that is a required component for knowing how to successfully make and use the instant method would prevent the skilled artisan from determining whether any modification of mutation to the specific human ERAB protein of SEQ ID NO: 2 could be made which retains the desired function of the instant invention, because any random mutation or modification manifested

within such a ERAB protein would be predicted to adversely alter its biologically active 3-dimensional conformation, and therefore, a method that the skilled artisan would not know how to make and/or use, without undue experimentation to determine otherwise.

In response, applicants respectfully traverse the Examiner's above rejection. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claims 1-19 and 23-25 without prejudice or disclaimer to applicants' right to pursue the subject matter of these claims in a later filed application. Therefore, applicants contend that regarding the ERAB polypeptide, the claims no longer recite the alleged limitation "or a variant thereof." Accordingly, applicants contend that this amendment obviates the Examiner's above rejection and respectfully request that the Examiner reconsider and withdraw such grounds of rejection.

Rejection under 35 U.S.C. §112, second paragraph:

The Examiner rejected claims 20 under 35 U.S.C. 112, second paragraph, as allegedly being incomplete for omitting essential steps, such omission amounting to gap between the steps. See MPEP § 2172.01. The Examiner alleged that the omitted steps are what the evaluation step recited in claim 20(c) entails. The Examiner suggested amending claim 20(c) to recite "wherein when the amount of amyloid-beta peptide bound to ERAB polypeptide is decreased in the presence of said agent, the ability of the agent to inhibit binding of ERAB polypeptide to amyloid-beta peptide is determined". The Examiner suggested that such amendment of claim 20 may obviate this rejection.

In response, applicants respectfully traverse the Examiner's above rejection. Nevertheless, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove amended claim 20.

In support, claim 20 now recites as follows:

" A method for evaluating the ability of an agent to inhibit binding of ERAB polypeptide to amyloid-beta peptide which comprises:

(a) incubating ERAB polypeptide, the agent and amyloid-beta peptide under suitable binding conditions;

(b) determining the amount of amyloid-beta peptide bound to ERAB polypeptide from the incubate of (a); and

(c) comparing the amount of bound amyloid-beta peptide determined in step (b) with an amount of amyloid-beta peptide bound to ERAB polypeptide determined in the absence of the agent, **wherein when the amount of amyloid-beta peptide bound to ERAB polypeptide is decreased in the presence of said agent,** the ability of the agent to inhibit binding of ERAB polypeptide to amyloid-beta peptide **is determined.**" [emphasis added].

Therefore, applicants have hereinabove amended claim 20(c) to more particularly point-out the metes and bounds of the presently claimed invention. Accordingly, applicants contend that this amendment obviates the Examiner's above rejection and respectfully request that the Examiner reconsider and withdraw such grounds of rejection.

Claim 21:

The Examiner rejected claim 21 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for using improper Markush language. The Examiner stated that elements within a Markush group are required to possess some structural similarity(e.g., be classified within the same class), which clearly is not the situation here. The Examiner stated for example, nucleic acids are class 536/23.1, while proteins are class 435.350, while the class of small molecules is unknown. See M.P.E.P. 2173.05 (h).

In response, applicants respectfully traverse the Examiner's above rejection. Applicants contend that claim 21 is not indefinite because each of the members of claim 21, i.e. a peptide, a peptidomimetic compound, a nucleic acid, or a small molecule, are defined as agents which specifically inhibit the intracellular binding between ERAB polypeptide and amyloid-beta peptide at the ERAB polypeptide active site. Therefore, each of these agents are disclosed in the specification and possess a common property which is mainly responsible for their function, i.e. the inhibition of ERAB/amyloid-beta binding via the ERAB active site.

In support, the specification recites that "a mutant of ERAB was created in which tyrosine (169) and lysine (173) were replaced by glycine. These two residues, tyrosine and lysine, are essential components of the active site of ERAB which is an enzyme." See page 45, lines 27-30. Further supporting the identification of the active site of the ERAB enzyme, the specification recites that "the mutant form is devoid of enzyme activity because enzyme assays for ERAB activity as an NAD-dependent short chain alcohol dehydrogenase (octanol as the substrate) showed no activity toward 17-beta-

estradiol (whereas native ERAB is an hydroxysteroid dehydrogenase)." See page 45, lines 34-38 and page 46, lines 1-2. Therefore, these data demonstrate the specific structure and function of the ERAB active site and its interaction with amyloid-beta peptide.

Therefore, applicants contend that each of the members of claim 21, i.e. a peptide, a peptidomimetic compound, a nucleic acid, or a small molecule, are agents which specifically inhibit the intracellular binding between ERAB polypeptide and amyloid-beta peptide, at the ERAB polypeptide active site. Therefore, each of these agents posses a common property which is mainly responsible for their function and claim 21 is not indefinite.

Summary

For the reasons set forth hereinabove, applicants respectfully quest that the Examiner reconsider and withdraw the various grounds of rejection and earnestly solicit allowance of the now pending claims, i.e. claims 20-21.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee, other than the enclosed $460.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

10/10/02

John P. White
Date
Reg. No. 28,678

Exhibit A:

--20. (Amended) A method for evaluating the ability of an agent to inhibit binding of ERAB polypeptide to amyloid-beta peptide which comprises:

(a) incubating ERAB polypeptide, the agent and amyloid-beta peptide under suitable binding conditions;

(b) determining the amount of amyloid-beta peptide bound to ERAB polypeptide from the incubate of (a); and

(c) comparing the amount of bound amyloid-beta peptide determined in step (b) with an amount of amyloid-beta peptide bound to ERAB polypeptide determined in the absence of the agent, [thereby evaluating] wherein when the amount of amyloid-beta peptide bound to ERAB polypeptide is decreased in the presence of said agent, the ability of the agent to inhibit binding of ERAB polypeptide to amyloid-beta peptide is determined.--

--26. (New) A composition comprising the agent of claim 20 and a pharmaceutically acceptable carrier.--